

TABLE 7-continued

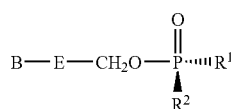
Excretion and Tissue Distribution of Radiolabelled GS-7340 in Dogs (Mean, N = 2) Following an Oral Dose at 10 mg-eq. PMPA/kg.					
Tissue/Fluid	GS-4331		GS-7340		Ratio of GS 7340 to GS-4331
	% Dose	Conc. (ug-eq/g)	% Dose	Conc. (ug-eq/g)	
Testes (L + R)	0.02	1.95	0.02	2.01	1.0
Skeletal Muscle	0.00	0.11	0.01	1.12	10.1
Heart	0.03	0.46	0.15	1.97	4.3
Femoral Bone	0.00	0.08	0.00	0.28	3.5
Bone Marrow	0.00	0.20	0.00	2.05	10.2
Skin	0.00	0.13	0.00	0.95	7.2
Abdominal fat	0.00	0.16	0.00	0.90	5.8
Eye (L + R)	0.00	0.06	0.00	0.23	3.7
Brain	0.00	<LOD	0.00	<LOD	n.d.
Cerebrospinal Fluid	0.00	<LOD	0.00	0.00	n.d.
Spinal Cord	0.00	<LOD	0.00	0.04	n.d.
Stomach	0.11	1.92	0.26	2.68	1.4
Jejunum	1.34	3.01	0.79	4.16	1.4
Duodenum	0.49	4.96	0.44	8.77	1.8
Ileum	0.01	0.50	0.16	4.61	9.2
Large Intestine	1.63	5.97	2.65	47.20	7.9
Gall bladder	0.00	3.58	0.04	25.02	7.0
Bile	0.00	9.63	0.22	40.48	4.2
Feces	40.96	n.d.	0.19	n.d.	n.a.
Total GI Tract Contents	5.61	n.d.	21.64	n.d.	n.a.
Urine	23.72	n.d.	14.73	n.d.	n.a.
Plasma at 24 h	0.00	0.20	0.00	0.20	1.0
Plasma at 0.25 h	n.a.	3.68	n.a.	3.48	0.9
PBMC*	0.00	n.d.	0.00	63.20	n.d.
Whole Blood	0.00	0.85	0.16	0.20	0.2
Total Recovery	81.10		68.96		

Calculated using typical recovery of  $15 \times 10^6$  cells total, and mean PBMC volume of 0.2 picoliters/cell

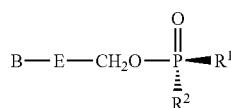
n.s.=no sample, n.a.=not applicable, n.d.=not determined.

The invention claimed is:

1. A method for antiviral therapy comprising administering a therapeutically effective amount of a diastereomerically enriched compound having the structure (3)



which contains less than 40% by weight of diastereomer (4)

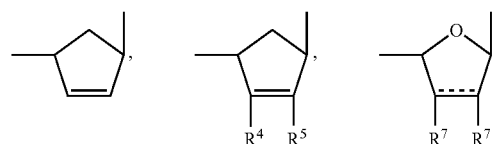


wherein  $\text{R}^1$  is an oxyester which is hydrolyzable in vivo, or hydroxyl;

B is a heterocyclic base;

$\text{R}^2$  is hydroxyl, or the residue of an amino acid bonded to the P atom through an amino group of the amino acid and having each carboxy substituent of the amino acid optionally esterified, but not both of  $\text{R}^1$  and  $\text{R}^2$  are hydroxyl;

E is  $-(\text{CH}_2)_2-$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2-$ ,  $-\text{CH}(\text{CH}_2\text{F})\text{CH}_2-$ ,  $-\text{CH}(\text{CH}_2\text{OH})\text{CH}_2-$ ,  $-\text{CH}(\text{CH}=\text{CH}_2)\text{CH}_2-$ ,  $-\text{CH}(\text{C}=\text{CH})\text{CH}_2-$ ,  $-\text{CH}(\text{CH}_2\text{N}_3)\text{CH}_2-$ ,



$-\text{CH}(\text{R}^6)\text{OCH}(\text{R}^6)-$ ,  $-\text{CH}(\text{R}^9)\text{CH}_2\text{O}-$  or  $-\text{CH}(\text{R}^8)\text{O}-$ , wherein the right hand bond is linked to the heterocyclic base;

the broken line represents an optional double bond;

$\text{R}^4$  and  $\text{R}^5$  are independently hydrogen, hydroxy, halo, amino or a substituent having 1-5 carbon atoms selected from acyloxy, alkoxy, alkylthio, alkylamino and dialkylamino;

$\text{R}^6$  and  $\text{R}^6$  are independently H,  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_1$ - $\text{C}_6$  hydroxyalkyl, or  $\text{C}_2$ - $\text{C}_7$  alkanoyl;

$\text{R}^7$  is independently H,  $\text{C}_1$ - $\text{C}_6$  alkyl, or are taken together to form  $-\text{O}-$  or  $-\text{CH}_2-$ ;

$\text{R}^8$  is H,  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_1$ - $\text{C}_6$  hydroxyalkyl or  $\text{C}_1$ - $\text{C}_6$  haloalkyl; and

$\text{R}^9$  is H, hydroxymethyl or acyloxymethyl;

and its salts, free base, and solvates.

2. The method of claim 1, wherein the diastereomerically enriched compound contains less than 20% by weight of the diastereomer (4).

3. The method of claim 2, wherein the diastereomerically enriched compound contains less than 5% by weight of the diastereomer (4).